REMARKS

A. Status of the Claims

Claims 1-19 are pending in the application. Claims 2, 4, 10, and 13 are indicated to be allowable if rewritten in independent form. Claims 1, 2, 4, 5, 8, 12, 15, and 18 have been amended. Claims 8 and 18 were amended to correct a typographical error. Claim 2 was amended to clarify the nucleotide sequence is transcribed from SEQ ID NO:1 (*see* Specification, p. 21, ln. 8-18). Claims 1, 4, and 12 were amended to delete the term "fifty-one." Additionally, claims 1 and 12 were amended to describe the skewed molar ratio in terms of the poorly represented nucleotide and to recite that the poorly represented nucleotide occurs 1 to 3 times in the random insert. Claims 5 and 15 were amended to maintain proper antecedent support. Support for these amendments may be found throughout the specification including, for example, at page 11, lines 12-17; page 13, lines 3-6; page 20, lines 17-19.

B. The Claims are Definite

Claims 1-19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. In particular, the Action identifies the following three phrases as allegedly rendering the claims indefinite: "about equal," "substantially comprise," and "chemically modified nucleotide." Applicant traverses this rejection.

The use of relative terminology, such as in the phrases "about equal" and "substantially comprise," in a claim is appropriate where one of ordinary skill in the art would understand what is claimed in light of the specification. MPEP § 2173.05(b). The rejection of the claims based on these terms is moot, however, in view of the amendments to claims 1 and 12. Current claims 1 and 12 recite that an A:C:G:T mole ratio of amounts of each nucleotide in said random insert is skewed such that one of the four nucleotides is poorly represented relative to the other three

nucleotides in said random insert and occurs 1 to 3 times in said random insert. In view of the teachings in the present specification, a person of ordinary skill in the art would understand what is meant by this phrase. In particular, the specification teaches that it is important to limit the number of labeled residues present in each aptamer in order to reduce the intrinsic fluorescent background (p. 20, ln. 10-16). This is accomplished by poorly representing the labeled nucleotide in the aptamer's random insert (p. 20, ln. 10 to p. 21, ln. 4). As recited in claim 3, for example, the mole ratio is skewed such that the mole ratio of the uridine is only 0.38, whereas the mole ratios of A, C, and G are 3:3:2, respectively. Additionally, the specification teaches that a signaling aptamer preferably bears only one to three labeled nucleotides (*see e.g.*, p. 11, ln. 12-14).

In regard to the term "chemically modified nucleotide," Applicant notes that claims may make use of the language understood by those of skill in the art without additional, detailed definitions in the written description. *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1556-58, 220 USPQ 303, 315-16 (Fed. Cir. 1983). Chemically modified nucleotides are well known to those in the art. For example, it is well known to those in the art to fluorescently label RNA molecules during transcription by incorporating chemically modified nucleotides as described in the present specification in the sentence bridging pages 23 and 24. It appears that the Examiner's concern may actually be with the breadth of this term. However, breadth of a claim is not to be equated with indefiniteness. MPEP § 2173.04 (citing *In re Miller*, 441 F.2d 689, 169 (CCPA 1971)).

C. Claims 1 and 2 are Novel over Winnacker

Claims 1 and 5 are rejected as anticipated by Winnacker *et al.* (U.S. Patent No. 6,426,409). Applicant traverses this rejection.

Winnacker fails to teach all of the limitations of current claims 1 and 5. In particular, Winnacker does not teach an RNA nucleic acid binding species having a nucleotide sequence including a random insert of nucleotides, wherein an A:C:G:T mole ratio of amounts of each nucleotide in said random insert is skewed such that one of the four nucleotides is poorly represented relative to the other three nucleotides in said random insert. Winnacker also fails to teach that the poorly represented nucleotide occurs 1 to 3 times in said random insert.

The Action states that Winnacker discloses an aptamer having a ratio of A, C, G, U of 18:15:32:18. The Action further states that it is inherent that the fourth nucleotide is labeled since the RNA was UTP labeled. The Action fails to establish that Winnacker teaches that one of the nucleotides is poorly represented in the random insert. In fact, according to the Action, the fourth nucleotide (U) is present in an amount equal to A and greater than C. Furthermore, current claim 1 states that the poorly represented nucleotide occurs 1 to 3 times in the random insert. According to the Action, Winnacker teaches that uridine occurs 18 times. For at least these reasons, a *prima facie* case of anticipation has not been established. Applicant, therefore, requests the withdrawal of this rejection.

D. The Claims are Patentable Over Winnacker in View of Huizenga and Jhaveri

The Action rejects claims 3, 6-7, 11-12, 14-17 and 19 under 35 U.S.C. § 103(a) as obvious over Winnacker in view of Huizenga *et al.* (*Biochem.*, 34:656-665 (1995)) in view of Jhaveri *et al.* (*J. Am. Chem. Soc.* 122:2469-2473 (2000)). Applicant traverses this rejection.

As discussed above, Winnacker does not teach all of the limitations of claims 1 and 5. Accordingly, the Action has not established a *prima facie* case of obviousness against these claims. If an independent claim is nonobvious under 35 U.S.C. § 103(a), then any claim

depending therefrom is nonobvious. MPEP § 2143.03. Claims 3, 6-7, and 11, therefore, are also nonobvious.

With regard to claim 12, the Action states that Huizenga discloses a DNA aptamer that binds adenosine and ATP in solution. The Action acknowledges that Huizenga does not disclose that the fourth nucleotide is labeled. The Action states that Jhaveri teaches that fluorescent dyes were placed adjacent to functional residues in aptamers, but the Action acknowledges that Jhaveri does not explicitly disclose that the fourth nucleotide is labeled. Nevertheless, the Action alleges that it would have been obvious to label the fourth nucleotide in view of the teachings of Huizenga and Jhaveri. This is insufficient to establish a *prima facie* case of obviousness.

As noted above, the Action admits that neither Huizenga nor Jhaveri teaches a labeled fourth nucleotide that is poorly represented in the random insert relative to the other three nucleotides. Furthermore, the Action fails to establish that these references teach or disclose that the DNA nucleic acid binding species has a skewed mole ratio of nucleotides such that one of the four nucleotides is poorly represented relative to the other three nucleotides in said random insert and occurs 1 to 3 times in said random insert. Thus, the Action has not met its burden of establishing a *prima facie* case of obviousness for these additional reasons.

In regard to claims 3 and 14, the Action admits that none of the references disclose the specific ratio of A:C:G:U or A:C:G:T recited in these claims. Nevertheless, the Action asserts that it would have been obvious to select the ratio of 3:3:2:0.38 to optimize the binding activity to the target. This assertion indicates a basic misunderstanding of the purpose of the ratio. This ratio is not for the optimization of target binding activity. The skewed molar ratio is to limit the number of labeled residues present in each aptamer in order to reduce the intrinsic fluorescent

background (p. 20, ln. 10-16). Improved target binding affinity, on the other hand, is achieved during the course of *in vitro* selection.

None of the references cited in the Action teach or suggest an RNA or DNA nucleic acid binding species having a skewed mole ratio of nucleotides such that one of the four nucleotides is poorly represented relative to the other three nucleotides in said random insert. Furthermore, none of the references teach or suggest that the poorly represented nucleotide occurs 1 to 3 times in the random insert, and that the poorly represented nucleotide is labeled. In view of the above, claims 3, 6-7, 11-12, 14-17 and 19 are nonobvious over Winnacker, Huizenga, and Jhaveri. Applicant, therefore, requests the withdrawal of this rejection.

E. The Claims are Patentable Over Winnacker in View of Huizenga, Jhaveri, and Heller

Claims 8 and 18 are rejected under 35 U.S.C. § 103(a) as obvious over Winnacker in view of Huizenga, Jhaveri, and further in view of Heller (U.S. Patent No. 5,849,489). The Action cites Heller as teaching fluorescein, Texas Red, and Rhodamine Green. Applicant traverses this rejection.

As discussed above, the Action fails to establish a *prima facie* case of obviousness in regard to claims 1 and 12, from which claims 8 and 18 depend. The alleged teachings of Heller regarding fluorescein, Texas Red, and Rhodamine Green do not address the deficiencies in claims 1 and 12 discussed above. If an independent claim is nonobvious under 35 U.S.C. § 103(a), then any claim depending therefrom is nonobvious. MPEP § 2143.03. In view of the nonobviousness of claims 1 and 12, claims 8 and 18 are also nonobvious. Applicant, therefore, requests the withdrawal of this rejection.

F. The Claims are Patentable Over Winnacker in View of Meade

Claim 9 is rejected under 35 U.S.C. § 103(a) as obvious over Winnacker in view of Mead *et al.* (U.S. Patent No. 5,591,578). The Action alleges that Mead teaches fluorescent dye labels on a uradine. Applicant traverses this rejection.

As discussed above, the Action fails to establish a *prima facie* case of obviousness in regard to claims 1 and 8, from which claim 9 depends directly or indirectly. The alleged teachings of Meade regarding the labeling of uradine does not address the deficiencies in claims 1 and 8 discussed above. If an independent claim is nonobvious under 35 U.S.C. § 103(a), then any claim depending therefrom is nonobvious. MPEP § 2143.03. In view of the nonobviousness of claims 1 and 8, claim 9 is also nonobvious. Applicant, therefore, requests the withdrawal of this rejection.

G. Conclusion

Applicant believe s this to be a complete reply to the Office Action dated April 5, 2007, and respectfully requests favorable consideration of the claims in view of the amendments and statements contained herein. The Examiner is invited to contact the undersigned attorney at (512) 536-5654 with any questions, comments, or suggestions relating to the referenced patent application.

Respectfully submitted,

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